Complete Summary

GUIDELINE TITLE

Cervical cancer: screening recommendations, with algorithms, for managing women with abnormal Pap test results.

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Cervical cancer: screening recommendations, with algorithms for managing women with abnormal Pap test results. Boston (MA): Brigham and Women's Hospital; 2004 Dec. 11 p. [11 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Brigham and Women's Hospital. Cervical cancer: screening recommendations, with algorithms, for managing women with abnormal Pap test results. Boston (MA): Brigham and Women's Hospital; 2002 Nov. 7 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Cervical cancer

GUIDELINE CATEGORY

Management
Prevention
Screening

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide physicians with clear guidelines for cervical cancer screening

TARGET POPULATION

- All women, including adolescents, who are sexually active
- All women over 21 years of age

INTERVENTIONS AND PRACTICES CONSIDERED

1. Papanicolaou (Pap) test (conventional and liquid-based Pap tests [ThinPrep®, SurePath®])
2. Tracking and reporting results
    - Bethesda system for reporting cervical cytology results
    - Patient notification and follow-up
    - Tracking system for results and follow-up
3. Appropriate responses to results (e.g., repeat Pap test, colposcopy, human papilloma virus [HPV] testing)

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches using Medline.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations for Screening

Whom to Test

- All women who are sexually active, starting within three years after onset of sexual activity
- All women over 21 years of age

Testing Frequency

- Adolescents to age 30: Adolescents may not be forthcoming about when they start sexual activity. In addition, patients in this age group are at higher risk for sexually transmitted disease and pregnancy. Because of all of these concerns, providers should have a low threshold for performing Papanicolaou (Pap) tests and pelvic exams in this age group. Screening should at least begin within three years after the initiation of sexual intercourse, but no later than age 21. Women should have a Pap test every year until age 30.
- Women over age 30, low risk: After age 30, women who have had three consecutive satisfactory and normal/negative Pap tests may be screened every two to three years if they do not have any of the following:
    - History of low-grade squamous intraepithelial lesion (LSIL) or high-grade squamous intraepithelial lesion (HSIL) (or cervical intraepithelial neoplasia [CIN] 2 or 3)
    - A compromised immune system
    - Human immunodeficiency virus (HIV) infection
    - Exposure to diethylstilbestrol (DES) in utero

More frequent screening at the provider's recommendation, or the patient's request, is also acceptable.

Note: In women aged 30 or over, the Food and Drug Administration (FDA) has recently approved a combined Pap/human papillomavirus (HPV) DNA test for primary screening. If a patient has the combined screen and tests negative, the screening interval should then be extended to three years. More frequent screening with the Pap/HPV combined test is not cost effective. The risk of cervical pre-cancer or cancer with less frequent screening, however, approaches that of no screening. Therefore, a clinician should opt for combined Pap/HPV screening only in the most compliant patients and if an excellent patient tracking system is in place. At the present time, the Pap/HPV screening option is not available at Brigham and Women's Hospital (BWH).

- Women over age 30 with previous abnormal Pap tests: Women over 30 years of age who have not had three consecutive satisfactory normal/negative Pap smears should continue to have Pap tests every one to two years, as they did before age 30. Women treated for LSIL or HSIL who have completed the appropriate post-treatment follow-up should be screened annually until at least three consecutive negative Pap results have been documented. Women who have had a hysterectomy and have a history of LSIL/HSIL (CIN2/3) should have Pap tests annually until three normal tests are documented, and then every two to three years thereafter.
- Women over age 30, higher risk: The following are co-factors for the development of intra-epithelial neoplasia. Therefore, if these are present, screening should be performed annually:
    - DES exposure
    - Prior abnormal Pap

    - Immune suppression (immunosuppressive illnesses or drugs, renal transplantation, HIV)
    - History of high-risk HPV type
    - Current smoking status
- Women with a history of hysterectomy: Meta-analyses suggest that there is no benefit to performing Pap tests on women who have had a hysterectomy for a benign cause, have no cervix, and have no history of vaginal or cervical neoplasia. Because mortality from cervical cancer is highest in women over the age of 65, and because of the difficulties in obtaining a reliable history and/or old records, caution should be used before terminating screening in these patients. Note that, although a patient may not need a Pap test, the pelvic examination is an important part of the annual examination and may be important in identifying ovarian or vaginal lesions, or bladder prolapse.

  Women who have had a hysterectomy should continue to have Pap tests under the following circumstances:

    - A history of HSIL prior to hysterectomy: obtain Pap tests every two to three years until 65 to 70 years old, then discontinue screening if three negative/normal Paps
    - Inadequate records regarding the reason for hysterectomy or results of previous Pap tests
- Older women: The American Cancer Society and the Society for Gynecologic Oncologists recommend that cervical cancer screening be discontinued in women over age 70 if they have had regular previous screenings with three normal Pap test results, and no abnormal tests in the previous 10 years. The United States Preventive Services Task Force recommends stopping at age 65 for women who have been regularly screened and have had consistently normal results. Nonetheless, women still need annual gynecologic histories and pelvic exams since the majority of other gynecologic cancers occur in this age group.

Note: Women of any age who have a new sexual partner may have had a new exposure to HPV infection. Clinicians may consider continuing annual Pap smears in these women, although there are not data at this time to support this practice.

<u>How to Perform a Pap Test</u>

1. The patient should not be actively menstruating. It is preferable that the patient refrain from sexual activity or use of vaginal medications or spermicides for the 48 hours prior to the test. Cervical irritation can lead to obscuring inflammation or reactive changes on the smear.
2. Insert appropriately sized bivalve speculum. Do not use lubricant jelly. Instead, use water for easier passage of the speculum.
3. If mucus or small amounts of blood are on the cervix, gently remove with a large cotton swab with a dabbing motion (to avoid removing cells from the transformation zone).
4. Scrape cervix with plastic spatula by inserting the larger irregularly shaped side of the spatula into the endocervix and turning 360 degrees, making sure to cover the entire transformation zone.
5. Insert endocervical brush into the os, no further than 3/4 of the length. Twist only 180 degrees to avoid bleeding.

6. The cervical broom is an alternative to the spatula and brush. Insert the longest bristles into the os and twist the broom around 360 degrees once.
7. If you are performing a liquid-based Pap test, swirl the sampling device in the fixative, occasionally scraping the cells from the brush into the liquid using the plastic spatula. Be sure to rinse the entire sample from the device. Cap, label, and send the sample vial to the laboratory for slide preparation.
8. If you are performing a conventional Pap smear, spread the cells from the spatula and the brush onto one slide, evenly, avoiding clumping. Immediately spray fixative at a distance of 12 inches, to avoid disrupting the cells.

The Liquid-Based Pap Test

Liquid based Pap tests (ThinPrep®, SurePath®) have been available for several years. One of these (ThinPrep®) is now commonly used at Bingham and Women's Hospital. Slides prepared from liquid based Pap tests contain less blood and fewer thick cell clumps. The test has higher sensitivity for detecting LSIL and HSIL and a higher rate of satisfactory specimens than the conventional Pap smear. This test has been approved by the FDA as a replacement for the traditional Pap test. A liquid-based Pap test costs approximately $12 more than a conventional Pap test and is covered by most insurers.

An additional benefit to using the liquid-based Pap test is that if the test returns with the result "Atypical Squamous Cells--Unknown Significance (ASC-US)", the residual liquid from the test can be used to run a DNA test for high-risk HPV types.

Evidence-based data indicate that both liquid-based and conventional Pap tests are acceptable methods for preparing slides for cervical cancer screening.

Pap Smear Results and Follow-up

The Bethesda System for Reporting Cervical Cytology Results

A Bethesda system report consists of two parts: "Adequacy of specimen" and "Descriptive diagnoses." The table below titled "Pap Test Results and Follow-Up" summarizes appropriate responses to results reported under the Bethesda system of classification.

Tracking and Reporting Results

- For a Pap test indicating cancer, notifying the patient within 72 hours is the standard of care.
- For precancerous lesions, promptly notify patient by phone or mail. The letter should include a full explanation of the finding. Include the physician's telephone number in the letter. Telephone calls should be documented.
- If patient does not comply with recommendations, a follow-up phone call is recommended and should be documented in the record.
- The physician's office should develop an efficient tracking system for Pap test results and follow-up.

- The physician or nurse practitioner should be sure to see all Pap test results before they are filed, and it should be noted in the file that the results were seen by the physician or nurse practitioner and appropriate action was taken.

Table: Pap Test Results and Follow-Up

	Reported Result	Appropriate Response
Adequacy of Specimen	Satisfactory for evaluation	See Descriptive Diagnoses
	Satisfactory but:	
	Obscuring inflammation, blood, or air-drying artifact (obscures 50 to 75% of slide, but still readable)	Consider treatment of reversible conditions (see below).
	No transformation zone (less than 10 endocervical or squamous metaplastic cells)	For Paps exhibiting obscuring factors (inflammation, blood, or air-drying artifact) or absence of a transformation zone, repeat Pap in 12 months unless patient has had insufficient prior screenings, history of recent positive high-risk HPV test, or history of abnormal Pap tests. In these cases, Pap test should be repeated within six months, but no earlier than six weeks.
	Unsatisfactory	
	Insufficient squamous component obscuring blood, inflammation, air drying artifact (>75% epithelial cells obscured)	Repeat Pap no earlier than 6 weeks. If patient is low risk and has had normal Pap tests for the previous 3 years consecutively, acceptable to repeat unsatisfactory Pap tests in one year.
Descriptive Diagnoses	Negative for intraepithelial lesion or malignancy	Repeat Pap in 1 to 3 years depending on risk status.
	Infection	
	Trichomonas vaginalis	Treat patient and partner with metronidazole, 2 grams, orally (po), 1 dose.
	Fungal organisms morphologically consistent with Candida species	Treat if symptomatic
	Shift in vaginal flora suggestive of bacterial vaginosis	Treat if symptomatic (i.e., if patient has symptoms of bacterial vaginosis).
	Bacteria consistent with Actinomyces species	Remove intrauterine device (IUD) if present and repeat Pap test in 3 months.
	Cellular changes associated with herpes simplex virus	Discuss with patient and provide appropriate information regarding transmission.
	Other non-neoplastic findings:	
	Inflammation	Treatment unnecessary if asymptomatic.
	Atrophy with inflammation	Treatment unnecessary if asymptomatic.

	Reported Result	Appropriate Response
	(atrophic vaginitis)	
	Intrauterine contraceptive device	No treatment necessary.
	Radiation	No treatment necessary.
	Other; or not otherwise specified	Treatment unnecessary if asymptomatic.
	Glandular cells status post-hysterectomy	No treatment necessary.
	Epithelial cell abnormalities Squamous cell	
	Atypical squamous cells (ASC). (5 to 7% of Pap tests)	Overall, there is a 5 to 17% chance of having high-grade cervical intraepithelial neoplasia (CIN) on biopsy with this diagnosis.
	ASC-US (atypical squamous cells, undetermined significance) *Suspicion of dysplasia not otherwise specified	Three appropriate management strategies: • Repeat cytology at 4- to 6-month intervals. Refer for colposcopy if any are ASC or more significant lesion. • Perform HPV testing on liquid from Pap test • Refer for colposcopy *Note: Immediate referral is recommended for women who are immunocompromised. **Note: For postmenopausal women, treat with 1 gram estrogen vaginal cream 3x a week for several weeks prior to a 3-month repeat Pap. Stop cream one week prior to the Pap.
	ASC-H (atypical squamous cells, cannot rule out HSIL) *Suspicion of high-grade dysplasia	Refer for colposcopy. There is a 24 to 94% chance of having cervical intraepithelial on biopsy.
	Low-grade squamous intraepithelial lesion (LSIL) (2% of Pap tests)	Refer for colposcopy. 10 to 18% reveal HSIL on colposcopy.
	High-grade squamous intraepithelial lesion (HSIL) (0.5% of Pap tests)	Refer for colposcopy and biopsy.
	Glandular Cell	
	Endometrial cells, cytologically benign	If age $\geq$40, clinical correlation is recommended. This finding in women who were within 10 days of onset of menses is less worrisome. For postmenopausal women, or women who were >10 days after onset of menses, consider referral to

	Reported Result	Appropriate Response
		gynecology for evaluation for consideration of endometrial biopsy. Any endometrial cells that are called "atypical" need immediate referral to gynecologist.
	Atypical glandular cells (AGC)--Less than 1% of Pap tests	
	Unqualified (endocervical endometrial, or "glandular cells not otherwise specified) (NOS)"	Refer to gynecologic oncology or gynecology for colposcopy, endocervical curettage, and endometrial biopsy (if >35 years or abnormal bleeding). Risk of cervical neoplasia is 9 to 54%; risk of invasive carcinoma 1 to 9%.
	Suggestive of neoplasia (endocervical, endometrial, or NOS)	Refer to gynecologic oncology. Risk of squamous intraepithelial neoplasia, adenocarcinoma in situ (AIS), or invasive cancer 27 to 96% • "Endocervical type" of AGC, favor neoplasia, carries a high probability (80%) of significant endocervical and/or squamous abnormality. • "Endometrial type" of AGC, favor neoplasia, carries about 50% chance of endometrial cancer.
	Adenocarcinoma in situ	Refer to gynecologic oncology. About 48 to 69% of patients will have AIS, and 38% will have invasive adenocarcinoma.
	Endocervical adenocarcinoma	Refer to gynecologic oncology.

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Management of Abnormal Pap Test Results
- Following Patients after Colposcopy

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

Guidelines are based on a comprehensive assessment of recent literature on cervical cancer screening.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate screening and management of abnormal Papanicolaou (Pap) results for the detection of cervical cancer

POTENTIAL HARMS

There is a significant false-negative rate in Papanicolaou (Pap) test results. One out of five women who have a significant lesion will have a negative Pap test.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guide is not intended to convey rigid standards. Instead, it should be tailored to the needs of each individual woman.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Brigham and Women's Hospital. Cervical cancer: screening recommendations, with algorithms for managing women with abnormal Pap test results. Boston (MA): Brigham and Women's Hospital; 2004 Dec. 11 p. [11 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 (revised 2004 Dec)

GUIDELINE DEVELOPER(S)

Brigham and Women's Hospital (Boston) - Hospital/Medical Center

SOURCE(S) OF FUNDING

Brigham and Women's Hospital

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Brigham and Women's Hospital. Cervical cancer: screening recommendations, with algorithms, for managing women with abnormal Pap test results. Boston (MA): Brigham and Women's Hospital; 2002 Nov. 7 p.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Brigham and Women's Hospital Web site.

Print copies: Available from the Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115. Telephone: (800) BWH-9999.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Brigham and Women's Hospital. The preventive step for cervical cancer: understanding Pap tests. Boston (MA): Brigham and Women's Hospital; 2004.

Electronic copies: Available from the Brigham and Women's Hospital Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

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